

Some Potential Interactions Between Prescribed Drugs and Over-the-Counter Drug Products

JACK N. TURNER, R.PH., A.B.D.P. *Palo Alto*

MUCH ATTENTION AND PUBLICITY has been given in recent years to the potential interactions between concurrently prescribed prescription drugs. Some interactions are antagonistic; some are synergistic; some are potentially lethal. However, in this context, the over-the-counter (OTC) drugs the patients use (and sometimes abuse) have been relatively ignored.

More medications are available for the relief of coughs and colds than for any other symptom. Hundreds of complex preparations for coughs, colds, hay fever and other respiratory conditions are available in super-markets, cigar stores and motel offices as well as in drug stores.

The ingredients include enzyme inducers (antihistamines), neuromuscular agents (anticholinergics), central nervous system stimulants or depressants, cardiovascular agents (decongestants), nephrotoxic agents (phenacetin) and other potent and toxic pharmacologic categories.

Many of these preparations can be abused by those seeking "kicks" and because they possess the potential for vast numbers of interactions with each other as well as with prescribed medications.

From Palo Alto Medical Clinic, Palo Alto.

Submitted August 17, 1971.

Reprint requests to: J. N. Turner, R.Ph., Palo Alto Medical Clinic, 300 Homer Avenue, Palo Alto, Ca. 94301.

Particular caution should be observed with monoamine oxidase inhibitors (MAOI), tricyclic antidepressants, and other hazardous interactants. Medications for respiratory disorders probably cause more problems than any other single class of therapeutic agents.

There is little, if any, documentation of the many potential interactions between prescribed drugs and OTC drug products. The accumulation of such information is a monumental task as the number of such products is in the thousands, and hundreds more appear every year.

The categories explored herein are internal analgesics, asthma preparations, nasal decongestants, cough and cold remedies, nasal sprays, cough mixtures and sleeping preparations. The tables are limited to the most popular, largest selling brands.

Some sources available to physicians who wish to keep abreast of potential drug interactions are MEDICAL LETTER, CLIN-ALERT, DRUG INTERACTIONS (Hansten, P., Lea & Febiger), HAZARDS OF MEDICATION (Martin, E., Lippincott), and THE HANDBOOK OF DRUG INTERACTIONS (Swidler, G., Wiley-Interscience). For formula and quantities the HANDBOOK OF NON-PRESCRIPTION DRUGS published by the American Pharmaceutical Association lists nearly all OTC products and their formulae that are sold in the United States.

TABLE I.—INTERNAL ANALGESICS: (salicylates as main ingredient)

<i>A Compound of One of These Products</i>	<i>(Active Ingredients)</i>	<i>When Taken with These Drugs</i>	<i>May Cause This Interaction</i>	<i>Comment and/or Mechanism of Action</i>
ASA COMPOUND*	aspirin phenacetin caffeine	227 mg 160 mg 32.5 mg	antidiabetics	hypoglycemia ¹
APC COMPOUND*	aspirin phenacetin caffeine	226 mg 162 mg 32 mg	alcoholic beverages	possible GI bleeding ²
ALKA-SELTZER†, **	aspirin calc. phosphate citric acid sod. bicarbonate	325 mg .196 mg 1.055 gm 1.904 gm	anticoagulants	salicylates potentiate effect of anticoagulants; response unpredictable when antihistamines are present. Also potentiated by acetaminophen.
ANACIN*	aspirin caffeine	400 mg 32.5 mg	CORTICOSTEROIDS	possible bleeding ^{3,4}
ANACIN ARTHRITIS FORMULA**	aspirin alum. hydroxide [*] mag. hydroxide [*]	500 mg	diphenylhydantoin	steroid effect potentiated ^{4,5}
ASCRIPTRIN**	aspirin alum. & mag. hydroxide [*]	300 mg	diphenylhydantoin	potentiation of di-phenylhydantoin ⁶
BUFFERIN**	aspirin alum. dihydroxyamino-acetate, 49 mg. mag. carb., 97 mg	324 mg	hypotensives	reversal of hypotensive
BROMO SELTZER†, **, §	pot. bromide sod. bicarb. & citric ac. [*]	162.5 mg	methotrexate	pancytopenia ⁷
CAMA**	aspirin mag. hydroxide alum. hydroxide	600 mg 150 mg 150 mg	oxyphenbutazone	diminished oxyphenbutazone effect ⁸
COPE*, **, ††	aspirin caffeine methaphenylene alum. hydroxide mag. hydroxide	420 mg 32 mg 15 mg 25 mg 50 mg	p-aminosalicylic acid phenobarbital phenylbutazone	salicylism ⁹ diminished effect of salicylates ⁹
DOAN'S PILLS	THEOBROMINE sod. salicyl. ¹⁰ Ext. Uva Ursi, [*] Ext. Buchu, [*] Vitamin A [*]		possible GI bleeding; water retention ^{11,12}	phenylbutazone inhibits the uricosuria that follows large doses of salicylates. Also may increase danger of GIT ulceration. Both drugs are ulcerogenic.
ECOTRIN	aspirin	300 mg (enteric coated)	PREDNISONE	rise in blood salicylate levels when prednisone is discontinued.
				salicylism ^{4,13}

EMPRIN COMPOUND*	aspirin phenacetin caffeine	233 mg 166 mg 30 mg	probenecid	probeneoid effect blocked*
EXCEDRIN*	aspirin caffeine salicylamide acetominophen	190 mg 60 mg 130 mg 90 mg	sulfisopyrazone	analgesic doses of salicylates may antagonize uricosuric effect.
FIZRIN†.**	aspirin* citric acid* sod. bicarbonate*			alkalinizing agents such as pot. cit. or sod. bicarb. may decrease urinary excretion; concomitant administration with antihistamines may produce atropinism (hazardous in glaucoma) by additive effect.
MEASURIN	aspirin (time release)	660 mg	tricyclic anti-depressants	
MIDOL*	aspirin caffeine cinnamyl ephedrine	450 mg 32 mg 15 mg	sulfisopyrazone effect diminished*, ¹⁰	
PAMPRINT†	phenacetin salicylamide pamabron pyralimine maleate	125 mg 125 mg 25 mg 25 mg	potentiated*, ¹⁵	
PERCOGESIC†	acetaminophen phenyltoloxamine cit.	325 mg 30 mg		
VANQUISH*.**	aspirin caffeine	227 mg 33 mg		* Caffeine may cause excitation response with MAOI; may reverse hypotensive drugs
	acetaminophen alum, hydroxide mag. hydroxide	194 mg 25 mg 50 mg		† Excess dosage may cause alkalosis, basic urine; amphetamine activity enhanced in basic urine due to decreased rate of excretion*, ¹⁹
ZUMARIN	salicylamide potass. salicylate	226 mg 230 mg		** May chelate or otherwise interfere with absorption of tetracyclines
				†† See Table 6 (antihistamines)
				§ Bromides taken with phenacetin over long periods may cause cyanosis; bromide intoxication associated with sulphhaemoglobinemia; the major hazard of phenacetin abuse is renal damage. ²⁰
				* Quantitative amounts not supplied

TABLE 2.—INHALATION PRODUCTS: (epinephrine as main ingredient)

<i>Any of These Products</i>	<i>(Active Ingredients)</i>	<i>When Taken with These Drugs</i>	<i>May Cause This Interaction</i>	<i>Comment and/or Mechanism of Action</i>
ADRENALIN	epinephrine HCl	.1%	furazolidone (after days of therapy acts as MAOI)	metabolism of norepinephrine is inhibited at storage sites, building up high blood-brain levels
ASTHMANEFRIN	epinephrine HCl (racemic)	.83%		
BRETHEASY	epinephrine HCl* (racemic)		MAOI	as above
BRONKAID MIST	epinephrine HCl	.5%	Digitalis glycosides	adrenergic drugs such as ephedrine and epinephrine may predispose patient to cardiac arrhythmias
MEDIHALER-EPI	epinephrine bitart	.7%	hypotensive drugs	reversal of effect of hypotensive agent possible through over-use
PRIMATENE MIST	epinephrine HCl	.5%	procarbazine (acts as MAOI)	metabolism of norepinephrine is inhibited at storage sites, building up high blood-brain levels
VAPONEFRIN	epinephrine HCl (racemic)	2.25%	insulin and oral antidiabetics sympathomimetics tricyclic anti-depressants	epinephrine may raise blood sugar levels by stimulating release of glycogen potentially lethal response unpredictable

TABLE 3.—LIQUID DECONGESTANTS, COUGH SUPPRESSANTS: (antihistamines and sympathomimetics as main ingredient)

<i>Any of These Products</i>	<i>(Active Ingredients)</i>	<i>When Taken with These Drugs</i>	<i>May Cause This Interaction</i>	<i>Comment and/or Mechanism of Action</i>
CHERACOL D*†§	dextromethorphan (per oz.) glyceryl guaiacolate amon. chlor.	60 mg 71 mg 518 mg	alcoholic beverage	CNS depression ^{16,23} enhanced sedation, additive effects: large amounts of alcohol may cause hypertension (potentiates adrenergic effects of sympathomimetics) (except Chercacol D)
COLDENE†§	phenylpropanolamine d-methorphan chlorpheniramine	11 mg 7.5 mg 1 mg	anticoagulants	antihistamines may cause reversal of anti-coagulant effect ^{11,24} acetaminophen may potentiate, response unpredictable

NOVAHISTINE††	phenylephrine chlorpheniramine	10 mg 2 mg	anticholinergics	atropinism, excessive dryness ^{8,19,22}
NOVAHISTINE-DH††	same as above plus codeine phos.	10 mg .6 gm/oz		
NYQUIL**§	acetaminophen ephed. sulf. doxylamine [*] d-methorphan [*] alcohol	25%	barbiturates	CNS depression ^{5,19}
SUPER ANAHIST SYR.§	thonzylamine ammon. chlor. d-methorphan	12.5 mg 100 mg 10 mg	DOXEPIN	sedation, atropinism ³
TRIAMINIC††	phenylpropanolamine pheniramine mal. pyrilamine mal. glyceryl guaiacolate	12.5 mg 6.25 mg 6.25 mg 100 mg	MAOI (see note § below re Nardil) [phenelzine]	sedation, atropinism ^{20,24}
TRIAMINICOL††§	same as above plus d-methorphan	15 mg	narcotics	sedation ³
TRIND††	phenylephrine HCl glyc. guaiacol. acetominophen	2.5 mg 50 mg 150 mg	reserpine	CNS depression ⁵
VICK'S FORMULA 44§	d-methorphan [*] doxylamine succ. [*]	sedatives and hypnotics steroids		CNS depression ⁵ decreased steroid effect ^{3,8}
		tranquillizers		CNS depression, atropinism (especially with phenothiazine ³)
				potentiation ²⁶
				tricyclic anti-depressants

*Quantitative amounts not supplied

^{*}Metabolic acidosis may result from overdosage

[†]Contains neither antihistamine nor sympathomimetic

^{**}Note: recommended dosage of NYQUIL is 30 cc, equivalent of 30 cc 50 proof alcoholic beverage

^{††}See Table 2, sympathomimetics

[§]Nardil (phenelzine) potentially lethal with d-methorphan²⁸

TABLE 4.—NASAL DECONGESTANTS: (antihistamines and sympathomimetics as main ingredients)

<i>Any of These Products</i>	<i>(Active Ingredients)</i>	<i>When Taken with These Drugs</i>	<i>May Cause This Interaction</i>	<i>Comment and/or Mechanism of Action</i>
ALLEREST*	phenylpropanolamine HCl pyramine mal. methapyrilene fumar.	50 mg 15 mg 10 mg	alcoholic beverages	CNS depression ^{16,23}
CONTAC**	phenylpropanolamine HCl chlorpheniramine mal. belladonna alkaloids	50 mg 4 mg .2 mg	anticoagulants	diminished effect of anticoagulant ^{11,24}
CORICIDIN*	chlorpheniramine mal. aspirin caffeine	.2 mg 390 mg 30 mg	anticholinergics	atropinism ^{6,18,22}
CORICIDIN-D*	same as Coricidin plus phenylephrine HCl	10 mg		
CORICIDIN DEMILET'S*	phenylephrine HCl chlorpheniramine aspirin	2.5 mg 0.5 mg 80 mg	antidiabetics	hyperglycemia ¹⁴
CORICIDIN MEDILET'S*	chlorpheniramine aspirin	5 mg 80 mg	barbiturates	sedation ^{5,19}
DRISTAN*†	phenylephrine HCl phenindamine tart. aspirin, [*] caffeine, [*] alum. hydpx., [*] mag. carb. [*]	5 mg 10 mg	doxepin	CNS depression, ³ atropinism
ORNEX*	phenylpropanolamine acetaminophen salicylamide caffeine	18 mg 175 mg 150 mg 15 mg	hypotensives	hypertension
SINTUTABS	phenylpropanolamine phenyltoloxamine cit. phenacetin acetaminophen	25 mg 22 mg 150 mg 150 mg	MAOI drugs	sedation, atropinism, hypertension ^{20,21}
SUPER ANAHIST*	phenylpropanolamine phenyltoloxamine cit. thonzonium HCl phenacetin aspirin caffeine, [*] ascorbic acid [*]	25 mg 6.25 mg 6.25 mg 97.2 mg 227 mg	levodopa narcotics procarbazine	hypertension ⁸ sedation ³ CNS depression, atropinism ^{20,21}

TRIAMINICIN*†	phenylpropanolamine pheniramine mal. pyrilamine mal. aspirin acetaminophen caffeine ascorbic ac. al. hydrox. gel (dried)	25 mg 12.5 mg 225 mg 150 mg 30 mg 50 mg 180 mg	reserpine	CNS depression, atropinism
URSINUS*	phenylpropanolamine pheniramine mal. pyrilamine mal. aspirin (equiv.)	25 mg 12.5 mg 12.5 mg 300 mg	sedatives and hypnotics steroid hormones tranquilizers	CNS depression ⁵ decreased hormone ^{3,8} effect
				CNS depression ³ (especially with phenothiazines) potentiation ²⁶
			tricyclic anti- depressant	sympathomimetic and tricyclic may be mutually potentiated

*Quantitative amounts not supplied

†Plus salicylates

†May contain tetracyclines (alum, cal., magn. ions)

*Belladonna contra-indicated in glaucoma

TABLE 5.—NASAL DECONGESTANTS (DROPS AND SPRAYS): # (antihistamines and/or sympathomimetics as main ingredients)

<i>Any of These Products</i>	<i>(Active Ingredients)</i>	<i>When Taken with Any of These Drugs</i>	<i>May Cause This Interaction</i>	<i>Comment and/or Mechanism of Action</i>
ALCONEFFRIN	phenylephrine (asst. strengths)	anticoagulants (with antihistamine containing drugs) digitalis	reversal of anti- coagulant ^{17,24}	over-use may decrease effect of anticoag- ulant (antihistamine content)
CONTAC SPRAY	phenylephrine methapyrilene	0.5% 0.2%	arrhythmias ^{13,25}	ephedrine and epinephrine combined with digitals glycosides predispose pa- tient to cardiac arrhythmias
CORICIDIN MIST	phenylephrine methapyrilene	0.5% 0.3%	furazolidone and MAO inhibitors, also procabarazine	due to possible inhibition of metabolism of sympathomimetic
NTZ	phenylephrine thenadil	0.25% 0.1%	hypertension, excitation ³	sympathomimetic may cause rise in blood sugar by stimulating release from liver of glycogen
NEO SYNEPHRINE	phenylephrine (asst. strengths)	insulin and oral anti- diabetic drugs	hyperglycemia ¹⁴	competitive α-adrenergic receptor block- ade
PRIVINE	naphazoline	0.5%	L-dopa	mydriatic effect of phenylephrine reduced ³ possible hypertension ³
SINEX	phenylephrine [*] methapyrilene [*]		hypertension ³	phenylephrine antagonizes hypotensive effect of phenothiazines
DRISTAN	phenylephrine [*] pheniramine [*]	phenothiazines	potentiation ²⁶	sympathomimetic and tricyclic may be mutually potentiated
VICK VATRONOL ⁺	ephedrine sulf. [*] methapyrilene [*]	tricyclic anti- depressants		

#This class of products is notorious for over-use, therefore included

*Quantitative amounts not given

+Digitals glycosides with epinephrine and related adrenergics may cause cardiac arrhythmias when over-used

TABLE 6.—SLEEPING AIDS: (*antihistamines as main ingredient*)

<i>Any of These Products</i>	<i>(Active Ingredients)</i>	<i>When Taken with Any of These Drugs:</i>	<i>May Cause This Interaction</i>	<i>Comment and/or Mechanism of Action</i>
DORMIN	methapyrilene	25 mg alcoholic beverage	CNS depression ^{16,22}	enhanced sedation due to synergistic activity of antihistamine with alcohol
NYTOL	methapyrilene salicylamide	25 mg 200 mg anticholinergics	atropinism ^{8,22}	antihistamines also have an anticholinergic effect
SLEEP EZE*	methapyrilene scopolamine	25 mg 0.125 mg anticoagulant	decreased anticoagulant effect ¹⁷	decreased by concomitant antihistamines
SOMINEX*	methapyrilene scopolamine salicylamide	25 mg 0.25 mg 200 mg barbiturates, sedatives, hypnotics, also reserpine	CNS depression ^{5,19}	barbiturate potentiated by antihistamines; may increase depth and duration of barbiturate narcosis
		doxepin	sedation, atropinism ³	additive effect
		narcotics	CNS depression ³	enhanced sedation by antihistamine
		MAOI	sedation, atropinism ^{20,21}	due to inhibition of metabolism
		steroid hormones	decreased steroid effect ^{1,8}	due to enzyme induction
		tricyclic anti-depressants	atropinism ²²	concomitant administration with antihistamines may produce atropinism (hazardous in glaucoma) by additive effect

*Contraindicated in glaucoma, asthma, hepatitis, and toxemia of pregnancy because of scopolamine content (salicylates not considered in this table. See Table 1.)

TRADE AND GENERIC NAMES OF PRESCRIPTION DRUGS REFERRED TO IN TABLES

Dialog,[®] *Tylenol*,[®] *Trind*,[®] acetaminophen
Dilantin,[®] diphenylhydantoin
Sinequan,[®] doxepin
Furoxone,[®] furazolidone
Larodopa,[®] *Dopar*,[®] levodopa
Eutonyl,[®] *Nardil*,[®] *Marplan*,[®] *Parnate*,[®] *Niamid*,[®]
Matulane,[®] MAOI
Tandearil,[®] oxyphenbutazone
Compazine,[®] *Mellaril*,[®] *Thorazine*,[®]
Phenergan,[®] *Sparine*,[®] *Stelazine*,[®] phenothiazines
Butazolidin,[®] *Butazolidin Alka*,[®] phenylbutazone
Benemid,[®] probenecid
Matulane,[®] procarbazine
Serpasil,[®] *Sandril*,[®] reserpine
Equanil,[®] *Miltown*,[®] (and meprobamate compounds),
Librium,[®] *Valium*,[®] *Serax*,[®] chloral hydrate,
Quaalude,[®] *Parest*,[®] *Dalmene*,[®] . . . sedatives, hypnotics
Anturane,[®] sulfonpyrazone
Aventyl,[®] *Elavil*,[®] *Norpramin*,[®] *Pertofrane*,[®] *Tofranil*,[®]
Triavil,[®] *Vivactil*,[®] *Etrafon*,[®] . . . tricyclic antidepressant

7. Azarnoff DL, Hurwitz A: Drug interactions. *Pharmacol Phys* 4:1-7, Feb 1970
8. Clark TH, Conney AH, Harpole BP, et al: Drug interactions that can effect your patients. *Patient Care* 1:33-77, Nov 1967
9. Conney AH: Microsomal enzyme induction by drugs. *Pharmacol Phys* 3:1-6, Dec 1969
10. Prescott LF: Pharmacokinetic drug interactions. *Lancet* 2:1239-1243, Dec 1969
11. Ellis J, Lawrence DR, et al: Modification by MAOI of the effect of some sympathomimetics on blood pressure. *Br Med J* 2:75-78, Apr 8, 1967
12. McIver AK: Drug incompatibilities. *Pharm J* 199:205-210, 344, 360, 548 Sep-Nov, 1967
13. American Hosp. Formulary Serv., Amer. Soc. Hosp. Pharmacists, Wash., D.C.
14. Hiatt N, Katz J: Modification of cardiac and hyperglycemic effects of epinephrine by insulin. *Life Sci* 8:551-558, 1969
15. Martin E: Hazards of medication—Drug Interactions. Lippincott, 1977 pp 415-420
16. Dunphy TW: The pharmacist's role in the prevention of adverse drug reactions (interactions). *Am J Hosp Pharm* 26:366-377 Jul 1969
17. Conney AH, et al: Adaptive increases in drug-metabolizing enzymes induced by phenobarbital and other drugs. *J Pharmacol Exptl Ther* 130:1-8, Sep 1960
18. Gershon H, Neubauer H, Sundland DM: Interaction between some anticholinergic agents and phenothiazines; potentiation of phenothiazine sedation and its antagonism. *Clin Pharmacol Ther* 6:749, Nov-Dec 1965
19. Burns JJ, Conney AH: Enzyme stimulation and inhibition in the metabolism of drugs. *Proc Roy Soc Med* 58:955-960, Nov 1965
20. Jori A: Potentiation of noradrenalin toxicity by drugs with anti-histamine activity. *J Pharm Pharmacol* 18:824, 1966
21. Goodman LS, Gilman A: *The Pharmacologic Basis of Therapeutics*. New York City, Macmillan Co., 1970, Sec V, pp 620-676
22. Goodman LS, Gilman A: *The Pharmacologic Basis of Therapeutics*. New York City, Macmillan Co., 1970, Sec IV, pp 402-619
23. Bester JF: Potentiation of drugs by ethyl alcohol. *Am Assoc Industrial Nursing J* 15:10, Aug 1967
24. Antiliz AM, et al: Potentiation of anticoagulant therapy by acetaminophen. *Curr Ther Res* 10:501-507, Oct 1968
25. Goodman LS, Gilman A: *The Pharmacologic Basis of Therapeutics*. New York City, Macmillan Co., 1970, Sec VI, pp 677-772
26. Hansten PD: Tricyclic antidepressants—Drug interactions. *Hosp Form Manag* 4:25-27, Oct 1969
27. Cairncross KD: On the peripheral pharmacology of amitriptyline. *Arch Int Pharmacodynam Ther* 154:438-448, 1965
28. Rivers N, Horner B: Possible lethal reaction between Nardil and d-methorphan. *Can Med Assoc J* 103:85, 1970
29. Side Effects of Drugs, Excerpta Medica Foundation. 1963, p 57
30. Milne MD: Influence of acid-base balance on efficacy and toxicity of drugs. *Proc Roy Soc Med* 58:961-963, Nov 1965

REFERENCES

1. Goodman LS, Gilman A: *The Pharmacologic Basis of Therapeutics*. New York City, Macmillan Co., 1970, Sec II, pp 369-370
2. Goulston K, Cooke AR: Alcohol, aspirin, and gastrointestinal bleeding. *Br Med J* 4:644-665, 1968
3. Manufacturers' package inserts (FDA approved)
4. Klinenberg JR, Miller F: Effect of corticosteroids on blood salicylate concentrations. *JAMA* 194: 601, 1965
5. Stuart DM: Drug metabolism—Part 2: Drug interactions. *Pharm Index* 10:4-16, Oct 1968
6. Lunde PK, Rane A, Yaffe SJ, et al: Plasma protein binding of phenylhydantoin in man. *Clin Pharmacol Ther* 11:846-855, 1970

STRAIGHT EYES OR BINOCULAR VISION—WHICH?

True or False: The restoration of single binocular vision in the patient with strabismus is the ultimate goal of all therapy.

False. I would like to go on record . . . saying that I think the cosmetic result is more important. It's the most important result for the parent, for the child, and ultimately for the ophthalmologist as well. However, I think we should strive to obtain binocular vision, too, because those patients who have singular binocular vision have the best-looking pair of eyes. Interestingly enough a number of years ago this concept was brought out in a big strabismus meeting in France. The French ophthalmologists who said that the cosmetic appearance was most important were butchered by the English and American ophthalmologists who said that binocular vision was the most important thing. As long as there is nobody else around but ophthalmologists, let's admit that the cosmetic result is the most important.

—EUGENE R. FOLK, M.D., Chicago
 Extracted from *Audio-Digest Ophthalmology*, Vol. 9, No. 15, in the Audio-Digest Foundation's subscription series of tape-recorded programs. For subscription information: 1930 Wilshire Blvd., Suite 700, Los Angeles, Ca. 90057